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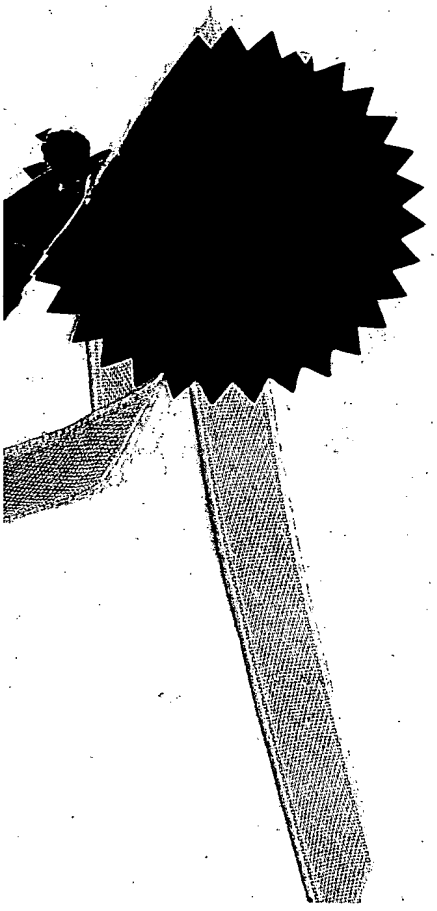

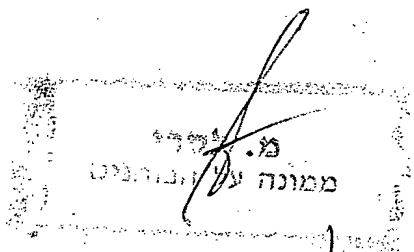

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חוק הפטנטים, התשכ"ז-1967
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בקשה לפטנט
Application for Patent

לשימוש הלשכה
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אני, (שם המבקש, מענו – ולגבי גוף מאוגד – מקום התאגדותו)
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טל./פקס 03-9697774

בעל אמצאה מכח עצמי דייר דניאל ים ששמה הוא:
Owner, by virtue of of an invention, the title of which is:

(בעברית) מיצוק שמנים ושימושם
(Hebrew)

(באנגלית) SOLIDIFICATION OF FLUID OILS AND THEIR USE
(English)

מבקש בזאת כי ינתן לי עליה פטנט.
hereby apply for a patent to be granted to me in respect thereof.

* בקשת חלוקה – Application for Division	* בקשת פטנט מוסף – Application for Patent of Addition	* דרישת דין קדימה Priority Claim		
מבקשת פטנט from Application	* לבקשה/לפטנט to Patent/Appl.	מספר/סימן Number/Mark	תאריך Date	מדינת האיגוד Convention Country
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Has been filed in case הוגש בענין

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חתימת המבקש
Signature of Applicant
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היום 22 בחודש אוקטובר שנת 1998
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SOLIDIFICATION OF FLUID OILS AND THEIR USE

מיצוק שמנים ושימושם

FIELD OF THE INVENTION

The present invention is in the field of substances used for nutrition, cosmetics or for treatment of diseases.

BACKGROUND OF THE INVENTION

Most fats which are nutritional substances exist as fluid oils. Their handling, storage and application is therefore limited to containers (e.g. cooking oil) or capsules (e.g. vitamine E). In principle, such oils can be handled in a solidified form by the addition of large excess of solids like starch, calcium carbonate, lactose etc, which is a common practice in the pharmaceutical industry.

Soft-solid mixtures which contain dietary oil at a concentration above 50% while the solidifying agent is biologically compatible, are not yet available and are the essence of this patent.

SUMMARY OF THE INVENTION

Physical solidification of oil (i.e. without changing its chemical composition), is important for handling and storage. At the current state of the art it can be achieved by mixing the oil with a solid material, where the additive is at a concentration higher than 50%.

In solidification of oils which are a nutrients or food additives, there is a need for a

solidifying agents which are either biological or biologically compatible.

This invention is constituted of solidified oils, where the solidifying agent is a biological or biologically compatible fat which when mixed with the oil can solidify it a surprisingly low percentage of less than 30%.

DESCRIPTION OF THE PREPARED EMBODIMENTS

The invention is illustrated below by the following non-limiting examples:

EXAMPLES

Example 1. Solidification of fish oil by bee wax.

80 gr bee wax (Colmeia do Mato Grosso, Mato Grosso, Brasil) was warmed at 80° C and mixed, under nitrogen atmospheres for several minutes with 400 gr fish oil (EPAX 7010 triglycerides, Pronova Biocare a.s. Sandefjord, Norway), while stirred mechanically to obtain a homogeneous mixture. Upon cooling to 25°C the mixture solified to form a homogeneous semi-solid paste. The weight percent of the fish oil in this mixture is 80%.

Example 2. Solidification of d-α-tocopherol (vitamine E) by sucrose polyester.

10 gr d-α-tocopherol (vitamine E) (Sigma, St. Louis Missouri) was mixed with 2 gr sucrose polyester (Olestra Procter and Gamble, Mason, Ohio) and warmed to 80°C

under nitrogen atmosphere to produce a homogenous mixture. Upon cooling to room temperature the mixture solidified. The weight percent of vitamine E in this mixture is 83%.

Example 3. Treatment of tumor bearing mice with solidified fish oil (SFO).

Based on our publication (Yam et al. Nutritional Bioch. 8:619-622,1977) we have tested the effect of solidified fish oil in the form presented in Example 1 on mice (C57BL/6J) bearing the well characterized Lewis Lung Carcinoma (3LL). The mice were kept in filter-covered plastic cages (10 mice per cage) and fed ad libitum with: basal oil-free standard diet supplemented with 5% of either (a) bee wax solidified soybean oil (SO), or (b) bee wax solidified fish oil (FO), as in example 1.

The ad libitum feeding with these diets started 2 weeks before tumor inoculation.

The tumor tested was a higly metastatic clone (D 122) of the 3LL Lewis Lung Carcinoma (Eisenbach L et al. Int J Cancer 32:113-120, 1983). Mice were inoculated in the footpad with 5×10^5 cells per mouse in 50 µl sterile phosphate buffered saline (PBS). Tumor size was monitored with a Varnier caliper. In accord with previous studies (Eisenbach et al., ibid), when local tumor reached a diameter of 8-9 mm, the tumor bearing leg was removed by amputation after ligation above the knee joint. Twenty eight days later the surviving mice were sacrified and lungs were assessed for metastatic load by weighing and histological examination.

Significantly slower growth of primary tumor, lower mortality rate and lower metastatic spread were observed in mice fed with SFO in comparison with mice fed

with SO.

The results of lung weights are summarized in Fig 1.

Example 4 Treatment of patients with hyperlipidemia with solidified fish oil (SFO).

Patients and methods

21 ambulatory patients, age 48-71 y. (15 men and 6 women), with hyperlipidemia were divided in two groups (test and control groups), took part in this study.

The test group, (10 men and 2 women) consumed 5 gr /d. of SFO in the form presented in Example 1, while the control group (7 patients) consumed the same amount of an isocaloric placebo in which the FO was replaced by olive oil.

Fasting blood samples were drawn at 0 and 42 d for analysis (see table 1 below).

Blood analysis- Part of the blood was transferred to precooled centrifuge tubes containing fluoride-oxalate and centrifugated at 1,500 r.p.m. during 10 min. and plasma was collected and frozen.

Triglycerides were determined by an enzymatic procedure with a commercial kit (Triglycerides Enzymatiques PAP 1000, Bio-Merieux, Charbonnieres-les-Bains,France).

Total cholesterol, was determined in serum by an enzymatic colourimeter method according to Siedel et al. (Clin. Chem. 29:1075,1983), (Monotest Cholesterol, Bohringer Diagnostica, GmbH, Mannheim, FRG).High-density lipoprotein (HDL) was analysed

according to Lopes-Virella et al. Clin. Chim. 23:882, 1977. Insulin level was determined in the serum by a double antibody radioimmunoassay, using ^{125} I- labelled human insulin (Pharmacia Diagnosis AB, Uppsala, Sweden). Glucose was determined according to Pennock et al ,Clin. Chi. Acta 48:193,1973.

The results are presented in Table 1.

Table 1

Mean ± S.D. values of plasma triglycerides, cholesterol, LDL-cholesterol insulin and glucose, before at day 0 and after 42 days.

	TEST GROUP		CONTROL GROUP	
	0 d.	42 d.	0 d.	42 d.
Triglycerides	240± 39	180± 18 mg/dl	230± 35	220± 42mg/dl
Cholesterol	270± 34	230± 19 mg/dl	280± 36	260 ± 28mg/dl
HDL-cholesterol	30± 12	48± 16mg/dl	32± 15	35± 17mg/dl
Insulin	31± 13	18± 8μU/ml	30± 14	31± 17μU/ml
Glucose	142± 18	95± 15mg/dl	128± 22	126± 22mg/dl

The results of the blood biochemistry presented in table 1 show that the SFO treatment induced a significant reduction in tryglycerides, cholesterol, insulin and glucose and an increase in HDL-cholesterol values at day 42 in comparison to 0 day. No significant changes were observed in the control group.

No negative side effects were observed in neither groups.

CLAIMS

1. Use of biologically compatible solid fats for the solidification of oils used for nutrition, cosmetics or medical treatments.
2. Use according to claim 1 wherein the solid fat is bee wax.
3. Use according to claim 1 wherein the solid fat is Propolis.
4. Use according to claim 1 wherein the solid fat is lanolin.
5. Use according to claim 1 wherein the solid fat is synthetic polyester of fatty acids and a natural saccharide.
6. Use according to claim 5 wherein the saccharide is sorbitol.
7. Use according to claim 5 where in the saccharide is glucose.
8. Use according to claim 5 wherein the solid fat is Olestra (a mixture of sucrose poly palmitate or poly stearate).
9. A soft-solid mixture comprised of 50% or more fish oil and 50% or less solid fat.
10. Use according to claim 9 wherein the solid fat is bee wax.
11. Use according to claim 9 wherein the solid fat is Propolis.

12. Use according to claim 9 wherein the solid fat is lanolin.

13. Use according to claim 9 wherein the solid fat is saccharide polyester appearing in claims 6,7 and 8.

14. A soft solid mixture comprised of 50% or more ethyl esters of natural fatty acids and 50% or less solid fat.

15. Use according to claim 14 wherein the solid fat is bee wax.

16. Use acording to claim 14 wherein the solid fat is Propolis.

17. Use according to claim 14 wherein the solid fat is lanolin.

18. Use according to claim 14 wherein the solid fat is saccharide polyester appearing in claims 6, 7 and 8.

19. Use of compositions described in claims 9-18 as food additive.

20. Use of compositions described in claims 9-18 for skin application.

21. Use of compositions described in claims 9-18 for the dietary treatment or prevention of cancer, hypertriglyceridemia, hypo HDL-cholesterol, hyperinsulinemia and hyperglycemia.

Fig. 1. Mean ± SD lung weight of mice after resection of primary growth and under SO or FO diet